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Advances in Critical Care/Emergency Medicine 2013

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Of the many publications in this field, the ones discussed hereunder seem to be most relevant for clinical practice.

Ischemic Stroke

Intravenous thrombolysis with tissue plasminogen activator (tPA) is the only therapy proven to improve outcome in ischemic stroke. Studies of intravenous thrombolysis show that response to therapy is time-dependent; the sooner the patients receive tPA, the better the chance of good outcome.¹

The required brain imaging before tPA administration delays the initiation of therapy because it necessitates patient transport. In the Pre-Hospital Acute Neurological Treatment and Optimization of Medical Care in Stroke (PHANTOM-S) pilot study, Weber et al² attempt to speed up stroke treatment by administering tPA before hospital arrival. When patients with presumed stroke contacted the emergency medical system, a stroke emergency mobile unit equipped with a CT scanner was dispatched. Brain imaging was performed at the scene, enabling tPA administration in the stroke emergency mobile unit. For patients in stroke emergency mobile unit, the median time between emergency call and initiation of tPA was 58 minutes (5–63); this time was 92 minutes (79–112) in a group of historic controls. The PHANTOM-S study was a nonrandomized study performed in urban Germany. A randomized controlled study performed in a more rural region of Germany showed a similar relative decrease in the time to tPA treatment among patients treated in a CT-equipped mobile stroke unit compared with those treated in the emergency room.³ These studies show that CT-equipped mobile stroke units decrease the time to tPA administration, which could translate into significant clinical benefit.

Hyperglycemia is associated with worse stroke outcome, but there is no evidence that strict glucose control improves outcome. In a proof-of-concept study to determine if aggressive glucose management could attenuate infarct growth, patients with carotid territory strokes were randomized to intensive insulin therapy (N=87) or standard (subcutaneous) insulin therapy (N=89) <6 hours after symptom onset.⁴ In the intensive insulin therapy group, insulin was administered as a continuous infusion with a goal glucose <7 mmol/L (<126 mg/dL) for a duration of 24 hours. MR images were obtained <5 hours after onset (before randomization) and again after cessation of therapy. Although the intensive insulin therapy regimen improved glucose control, it was associated with increased infarct growth. The intensive insulin therapy regimen also led to an increase in hypoglycemia episodes. Clinical outcomes were similar between the treatment groups. The ongoing Stroke Hyperglycemia Insulin Network Effort (SHINE) trial aims for a similar glucose goal in the intensive treatment arm (80–130 mg/dL), but allows for 12 hours between symptom onset and initiation of treatment.⁵

Notwithstanding SHINE, the abundance of data to date suggests that intensive insulin therapy in acute stroke is of no benefit and may cause harm.

Intracerebral Hemorrhage

After the Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT1) pilot study, the larger INTERACT2 study tested whether rapid lowering of blood pressure (target systolic <140 mm Hg within 1 hour of randomization and maintained for 7 days)⁶ improves outcome in patients with intracerebral hemorrhage (ICH) compared with current guideline-recommended treatment (target systolic <180 mm Hg).⁷ Patients were treated <6 hours after symptom onset; exclusion criteria included structural causes for bleeding, deep coma (median Glasgow Coma Scale, 14), massive hematomas (median volume, 11 mL), poor prognosis, and plans for immediate surgery. Among 2794 patients for whom the primary outcome (modified Rankin Scale) could be determined at 90 days, average enrollment blood pressure was 179/101 mm Hg. Systolic blood pressure 1 and 6 hours after treatment was 150 and 139 mm Hg with intensive therapy versus 164 and 153 mm Hg with conventional treatment. The primary outcome (death or major disability) did not differ between groups. Ordinal analysis of modified Rankin Scale scores, however, indicated that participants in the intensive treatment group had significantly improved functional outcomes with better overall health-related quality (EQ-5D score; P=0.002). Limitations of INTERACT2 are noted; particularly neither antihypertensive medication nor clinical management was standardized in the acute phase. The ongoing Antihypertensive Treatment of Cerebral Hemorrhage (ATACH II) trial will provide further data on intensive lowering of blood pressure <4.5 hours using intravenous nicardipine.⁸ Despite the negative primary end point, INTERACT2 shows that rapid blood pressure lowering is safe and may improve functional outcome in a select subgroup of patients with relatively mild symptoms/small hemorrhages. Targeting a systolic blood pressure value <140 mm Hg is justifiable in this patient population with spontaneous ICH.

The Surgical Trial in Lobar Intracerebral Hemorrhage (STICH) II study compared early surgery with initial conservative treatment in an international multicenter trial.⁹ Only conscious patients with superficial lobar

ICH between 10 to 100 mL and no intraventricular hemorrhage admitted <48 hours after symptom onset were included. Of the 601 patients enrolled, 307 were randomly assigned to early surgery and 294 to initial conservative treatment. In the group randomized to initial conservative treatment, delayed evacuation was permitted if judged clinically appropriate. Unfavorable outcome (based on extended Glasgow Outcome Scale) was seen in 59% of the early surgery group patients and in 62% of the initial conservative treatment group (odds ratio, 0.86; $P=0.367$). Of the patients randomized to initial conservative treatment, 21% eventually went on to surgery. The absence of a significant difference between the groups may be related to the heterogeneous patient population (i.e., hematoma volumes ranging from 10 to 100 mL), a high crossover rate from initial conservative treatment to surgery, and lack of standardized procedures for both surgical intervention and conservative treatment. Early surgery may be only one important therapy for the treatment of patients with ICH. The ongoing Clot Lysis Evaluating Accelerated Resolution of Intraventricular Hemorrhage (CLEAR-IVH) and Minimally Invasive Surgery Plus tPA for ICH Evacuation (MISTIE) trials will show whether minimally invasive techniques could play a role in the treatment of subsets of ICH patients.

Cardiac Arrest

After 2 seminal studies that showed that hypothermia improves outcome, hypothermia has become a standard of care for the treatment of patients with cardiac arrest due to ventricular fibrillation. It has since been hypothesized that earlier cooling would result in better outcome. In a study by Kim et al,¹⁰ patients with cardiac arrest were randomized to pre-hospital cooling with infusion of chilled (4°C) saline versus standard of care during a 5-year period. The study included all patients with cardiac arrest regardless of initial rhythm; the goal temperature for cooling was $\leq 34^{\circ}\text{C}$. The primary analysis included 1359 patients. For patients who also received hospital cooling, the administration of cooled saline in the pre-hospital setting reduced the time to goal temperature by more than an hour (4.2 versus 5.5 hours; $P<0.001$). Pre-hospital cooling, however, did not decrease mortality or improve neurological outcome at the time of hospital discharge. Furthermore, patients treated with chilled saline in the field were more likely to have a rearrest and evidence pulmonary edema at hospital admission. A separate study casts doubt on the benefit of hypothermia in patients with out-of-hospital cardiac arrest.¹¹ In a randomized controlled study comparing 2 temperature goals, Nielsen et al¹¹ found no decrease in mortality or improvement in neurological outcome in patients randomized to hypothermia (33°C) compared with those where the focus was to avoid fever (36°C). These trials suggest that decreasing the time to achieve hypothermia confers no benefit. Moreover, the value of hypothermia itself is questioned. Additional studies will be needed to determine the true value of hypothermia after cardiac arrest, appropriate temperature targets, duration of therapy, and methods for cooling.

Disclosures

None.

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